c) Remarks

Claims 1-4 are pending in this application. Claims 3 and 4 have been withdrawn from consideration. Claims 1-2 have been amended in various particulars as indicated hereinabove. Claims 5-7 are new.

With regard to the amendment of the specification, Applicants explain that there was a typo in the translation of the original PCT application into English. In the PCT publication the range is "1185-1205", while the translation accidentally entered the range as "1185-1295". The referenced amendment to the specification corrected that typo.

Claims 1 and 2 were rejected under 35 U.S.C. 112, second paragraph.

Applicants believe that the claims as amended are in compliance with 35 U.S.C. 112, second paragraph. In particular, it has been clarified that the claimed medicament comprises one or more homeopathic dilutions. Illustrative Example 1 in the specification discloses three homeopathic dilutions used in a treatment regimen. Illustrative Example 2 in the specification describes three homeopathic dilutions administered to a patient. Illustrative Example 3 describes a medicament comprising three homeopathic dilutions administered to a patient.

With regard to the terms "homeopathic dilutions of the potentiated...antibodies" now present in the Claims, Applicants provide the following explanation. The Patent Office is asked to refer to the report on "Q&A about Homeopathy", issued by the National Center for Complementary and Alternative Medicine of the National Institute of Health (NIH) (copy enclosed). On page 2 of the enclosed copy, the NIH report explains (emphasis added):

"In the late 1700s, Samuel Hahnemann, a physician, chemist, and linguist in Germany, proposed a new approach to treating illness."

"Hahnemann added two additional elements to homeopathy:

- A concept that became **"potentization,"** which holds that systematically diluting a substance, with vigorous shaking at each step of dilution, makes the remedy more, not less, effective by extracting the vital essence of the substance. If dilution continues to a point where the

substance's molecules are gone, homeopathy holds that the "memory" of them--that is, the effects they exerted on the surrounding water molecules--may still be therapeutic.

- A concept that treatment should be selected based upon a total picture of an individual and his symptoms, not solely upon symptoms of a disease. Homeopaths evaluate not only a person's physical symptoms but her emotions, mental states, lifestyle, nutrition, and other aspects. In homeopathy, different people with the same symptoms may receive different homeopathic remedies.

Hans Burch Gram, a Boston-born doctor, studied homeopathy in Europe and introduced it into the United States in 1825. European immigrants trained in homeopathy also made the treatment increasingly available in America. In 1835, the first homeopathic medical college was established in Allentown, Pennsylvania. By the turn of the 20th century, 8 percent of all American medical practitioners were homeopaths, and there were 20 homeopathic medical colleges and more than 100 homeopathic hospitals in the United States. "

As follows from the above, the concept of potentization as extreme dilution and that a remedy is prepared by extremely diluting the substance in a series of steps has been known and well defined in the US since at least the first half of the 19th century. Homeopathy asserts that this process can maintain a substance's healing properties regardless of how many times it has been diluted. Many homeopathic remedies are so highly diluted that not one molecule of the original natural substance remains in the dilution. Potentiated diluted remedy is believed (without being committed to any specific scientific theory) to have modified properties of the solvent molecules or the clusters of the solvent molecules to cause therapeutic effect. While no definite scientific theory exists to explain how potentiated remedies work, it has been known that they work, along with the well known term "potentiated", defining such remedies. Please refer to the Rule 132 Declaration of inventor Oleg Epshtein providing additional experimental data on the efficacy of the claimed medicament and the research behind those data. The introduced Claim amendments are also supported by paragraphs [0005] and [0014] of the specification as published.

The present amended Claims now also refer to "one or more homeopathic dilutions of the potentiated polyclonal or monoclonal antibodies to the NO synthase being obtained according to homeopathic technology". Homeopathic dilutions and homeopathic technology have been known in the field of homeopathy in the US to anyone of average skill in that field for almost 200 years, as written in the referenced NIH report. Paragraph [0014] of the specification as originally filed describes the homeopathic potentiation technology of producing homeopathic dilutions (decimal dilutions and centesimal

dilutions, as well as simultaneous shaking). Additionally, enclosed with this response is a PDF file is a copy of the English language translation of the German Homeopathic Pharmacopoeia (1978, British Homeopathic Association, 5th Supplement of 1991), which has extensive description of the potentization technique and various types of homeopathic dilutions. Applicants believe that the proposed amendments alternatively define the claimed invention in a precise and definite manner.

Claims 1 and 2 were rejected under 35 U.S.C. 103(a) over Salerno (US Patent No. 6,150,500) in view of Davenas *et al.*, Epshtein *et al.*, and Feldman *et al.* (US Patent No. 5,741,488). This rejection is respectfully traversed for the following reasons.

For an obviousness rejection to be proper, the Patent Office must meet the burden of establishing a prima facie case of obviousness. The Patent Office must meet the burden of establishing that all elements of the invention are disclosed in the cited publications, which must have a suggestion, teaching or motivation for one of ordinary skill in the art to modify a reference or combined references.[1] The cited publications should explicitly provide a reasonable expectation of success, determined from the position of one of ordinary skill in the art at the time the invention was made.[2]

The Patent Office wrote that "Salerno teaches antibodies to endothelial nitric oxide synthase (eNOS) and their methods of production." Applicants respectfully bring to the attention of the Patent office the fact that the Salerno patent teaches antibodies that bind to the enzyme. For example, in Col. 8, lines 16-34 Salerno discloses (emphasis added):

> Agents which modulate NOS enzyme activity include agents having an array of positively charged residues or molecules, such as the array of positively charged amino acids in ENOS-homologous peptides. This agent can modulate an NOS enzyme activity by effecting electron transport between NADPH and the active site of an NOS enzyme. Other agents have at least one functional group, and may have two or more functional groups, which bind to the INOS-specific peptide; or have at least one functional group, and may have two or more functional groups,

1 In re Lee, 277 F.3d 1338, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002).
2 In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970); Amgen v. Chugai Pharmaceuticals Co., 18 U.S.P.Q.2d, 1016, 1023 (Fed. Cir. 1996).

> which bind to the recognition site of the inhibitory peptide in a constitutive NOS enzyme, or a homologous region in inducible NOS, and thereby modulate INOS activity.

Furthermore, in Col. 8, lines 43-45 of the Salerno patent it is disclosed (emphasis added):

> Representative agents include antibodies for the synthetic peptide analogs of the NOS control elements and neighboring structural elements.

Contrary to the disclosure of the Salerno patent, the present invention as claimed in amended independent Claim 1 specifies that potentiated form of antibodies to an endothelial nitric oxide synthase (NO synthase) prepared s homeopathic dilutions do not bind the NO synthase. As disclosed in paragraph [0010] of the specification supporting Claim 1:

> Unlike physiologic (therapeutic) doses of the antibodies, the activated forms of ultra-low doses of the antibodies to NO synthase do not bind (inactivate) the enzyme; instead, they modify its effects. The new medication has an effect synergic with that of NO synthase. The existence of the therapeutic effect of ultra-low doses of antibodies activated by homeopathic technology, as well as the unidirectional character of the action with the original enzyme do not follow from the state-of-the-art knowledge and have been discovered by the inventor.

Therefore, the Salerno patent does not teach the homeopathic dilutions of potentiated form of antibodies that are non-binding with the enzyme.

The Davenas and Epshtein articles and the Feldman patent cited by the Patent Office do not cure the deficiency of disclosure of the Salerno patent.

In the Devenas article the potentiated antibodies to IgE, which are completely different antibodies, were used to change the rate of basophile degranulation. Nowhere in the Davenas article were there disclosed the antibodies to the claimed antigen, taught or suggested. No teaching of the homeopathic dilutions of potentiated form antibodies that are non-binding with the enzyme could be found in the Davenas article either.

In the Feldman patent considers lowering the dosage of the antibodies in order to make the cheaper. That patent had no disclosure of the homeopathic dilutions

(homeopathic doses) of the potentiated antibodies prepared by homeopathic technology. The degrees of dilution in Feldman are not homeopathic dilutions (not decimal or centesimal dilutions), so no homeopathic dilutions of potentiated form of antibodies non-binding to a specific enzyme NO synthase are disclosed in the Feldman patent either.

In the cited Epshtein article there is no disclosure of the potentiated form antibodies to the specific antigen – NO synthase – and no disclosure in that article teaches or suggests a medicament based on any kinds of antibodies. That article does not disclose the homeopathic dilutions of potentiated form of antibodies that are non-binding with the specific enzyme.

Furthermore, none of the cited publications discloses a medicament effective for treating erectile dysfunction and comprised of homeopathic dilutions as claimed in amended independent Claim 1 and new Claim 6. To further support this aspect of the invention, Applicants enclose additional evidence of efficacy of the claimed medicament in the form of an enclosed Declaration of inventor Oleg Epshtein under 37 CFR 132. Applicants also assert that the non-obviousness of the claimed invention is additionally supported by the data of solid commercial success, as reflected in the enclosed Declaration of inventor Oleg Epshtein under 37 CFR 132. Therefore, Applicants respectfully assert that amended independent Claim 1 and its dependent Claim 2 and 5 comply with the requirements of 35 U.S.C. 103(a) and are patentable over the cited publications.

Applicants bring to the attention of the Patent Office that new Claim 6 defined the invention as comprised of one or more homeopathic dilutions of potentiated form of monoclonal, polyclonal, or natural antibodies to a synthetic polypeptide corresponding to a fragment 1185-1295 of an animoacid sequence of an endothelial Type III nitric oxide synthase (NO synthase) that do not bind the NO synthase. None of the cited publications contains a disclosure of the potentiated form of antibodies to a specific polypeptide of the NO synthase. Applicants respectfully assert that new Claim 6 and its dependent Claim 7

comply with the requirements of 35 U.S.C. 103(a) and are patentable over the cited publications.

It is believed that the present application is in condition for allowance. A Notice of Allowance is respectfully solicited. Should any questions arise, the Examiner is encouraged to contact the undersigned.

Respectfully submitted,

HOUSTON ELISEEVA LLP

By /Maria Eliseeva/
Maria M. Eliseeva
Registration No.: 43,328
Tel.: 781 863 9991
Fax: 781 863 9931

4 Militia Drive, Suite 4
Lexington, Massachusetts 02421
Date: January 9, 2008